

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C.20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

<b>Date of mailing (day/month/year)</b> 31 March 2000 (31.03.00)	<b>Applicant's or agent's file reference</b> UPN-3696
<b>International application No.</b> PCT/US99/15062	<b>Priority date (day/month/year)</b> 01 July 1998 (01.07.98)
<b>International filing date (day/month/year)</b> 01 July 1999 (01.07.99)	
<b>Applicant</b> MURALI, Ramachandran et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

31 January 2000 (31.01.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was  
☐ was not

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made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<b>The International Bureau of WIPO</b> 34, chemin des Colombettes 1211 Geneva 20, Switzerland	<b>Authorized officer</b>  Juan Cruz
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

# PCT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

RECEIVED

OCT 19 2000

To: JOHN J. MACKIEWICZ  
WOODCOCK WASHBURN KURTZ MACKIEWICZ &  
NORRIS LLP  
ONE LIBERTY PLACE - 4TH FLOOR  
PHILADELPHIA, PA 19103

**PCT** Woodcock Washburn Kurtz & Norris LLP

## NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

RECEIVED

OCT 19 2000

DOCKET DEPT.  
WWKMN

Date of Mailing  
(day/month/year)

13 OCT 2000

Applicant's or agent's file reference

UPN-3696

### IMPORTANT NOTIFICATION

International application No.

PCT/US99/15062

International filing date (day/month/year)

01 JULY 1999

Priority Date (day/month/year)

01 JULY 1998

Applicant

THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

EVERETT WHITE

Telephone No. (703) 308-1235

# PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

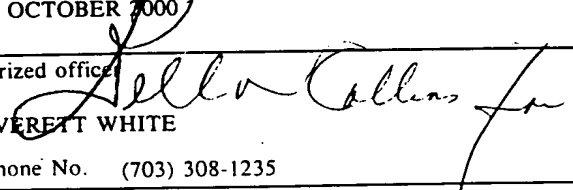
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference UPN-3696	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US99/15062	International filing date (day/month/year) 01 JULY 1999	Priority date (day/month/year) 01 JULY 1998
International Patent Classification (IPC) or national classification and IPC IPC(7): C07K 3/00 and US Cl.: 530/350		
Applicant THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA		

- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 5 sheets.  
☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).  
These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 31 JANUARY 2000	Date of completion of this report 02 OCTOBER 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer  EVERETT WHITE
Facsimile No. (703) 305-3230	Telephone No. (703) 308-1235

## I. Basis of the report

## 1. With regard to the elements of the international application:\*

☒ the international application as originally filed☒ the description:

pages 1-81, as originally filed

pages NONE, filed with the demand

pages NONE, filed with the letter of

☒ the claims:

pages 82-83, as originally filed

pages NONE, as amended (together with any statement) under Article 19

pages NONE, filed with the demand

pages NONE, filed with the letter of

☒ the drawings:

pages 1-4, as originally filed

pages NONE, filed with the demand

pages NONE, filed with the letter of

☒ the sequence listing part of the description:

pages NONE, as originally filed

pages NONE, filed with the demand

pages NONE, filed with the letter of

## 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).☐ the language of publication of the international application (under Rule 48.3(b)).☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

## 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.☐ filed together with the international application in computer readable form.☐ furnished subsequently to this Authority in written form.☐ furnished subsequently to this Authority in computer readable form.☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4. ☒ The amendments have resulted in the cancellation of:☒ the description, pages NONE☒ the claims, Nos. NONE☒ the drawings, sheets/fig. NONE5. ☒ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 2-5

because:

☐ the said international application, or the said claim Nos. \_ relate to the following subject matter which does not require international preliminary examination (*specify*).

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_ are so unclear that no meaningful opinion could be formed (*specify*).

☐ the claims, or said claims Nos. \_ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 215

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. statement**

Novelty (N)

Claims	<u>NONE</u>	YES
Claims	<u>1</u>	NO

Inventive Step (IS)

Claims	<u>NONE</u>	YES
Claims	<u>1</u>	NO

Industrial Applicability (IA)

Claims	<u>1</u>	YES
Claims	<u>NONE</u>	NO

**2. citations and explanations (Rule 70.7)**

Claim 1 lacks novelty under PCT Article 33(2) as being anticipated by Fred et al (US Patent No. 5,597,719).

Applicants claim a method of identifying a compound that modulates intermolecular interactions between a target protein and a modifier.

The Freed et al patent discloses intermolecular interactions between Raf-1 and human 14-3-3 proteins which regulate Raf activity that anticipates the instantly claimed method. The Freed et al patent describes a method wherein agents are tested for their ability to alter binding between a raf-1 polypeptide and a raf-1-interacting 14-3-3 polypeptide under suitable assay binding conditions. One means for detecting binding of a raf-1 polypeptide to a raf-1 interacting 14-3-3 polypeptide is to immobilize the raf-1 polypeptide, such as by covalent or noncovalent chemical linkage to a solid support, and to contact the immobilized raf-1 polypeptide with raf-1-interacting 14-3-3 polypeptide that has been labeled with a detectable marker. In one variation, the binding assay is performed with soluble raf-1 and raf-1-binding 14-3-3 polypeptides and the resultant bound complexes are separated from unbound raf-1 and raf-1-binding polypeptides, and the bound complexes are quantitated. Agents that inhibit or augment the formation of bound complexes as compared to a control binding reaction lacking agent are thereby identified as raf-1-modulating agents and are candidate therapeutic agents (see column 7, line 66 to column 8, line 31). The above described method of the Freed et al patent anticipates claim 1 under PCT Article 33(2).

----- NEW CITATIONS -----

NONE

**Supplemental B x**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**I. BASIS OF REPORT:**

5. (Some) amendments are considered to go beyond the disclosure as filed:

NONE

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference UPN-3696	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US99/15062	International filing date ( <i>day/month/year</i> ) 01 JULY 1999	(Earliest) Priority Date ( <i>day/month/year</i> ) 01 JULY 1998
Applicant THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☐ Certain claims were found unsearchable (See Box I).
  
2. ☒ Unity of invention is lacking (See Box II).
  
3. ☐ The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing
 

☐ filed with the international application.  
☐ furnished by the applicant separately from the international application,  

☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.

☐ transcribed by this Authority.
  
4. With regard to the title,
 

☒ the text is approved as submitted by the applicant.  
☐ the text has been established by this Authority to read as follows:
  
5. With regard to the abstract,
 

☒ the text is approved as submitted by the applicant.  
☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
  
6. The figure of the drawings to be published with the abstract is:  
 Figure No. \_\_\_\_\_
 

☐ as suggested by the applicant.  
☐ because the applicant failed to suggest a figure.  
☐ because this figure better characterizes the invention.

☒ None of the figures.



## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/15062

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(6) :C07K 3/00

US CL :530/350

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 530/350

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

MEDLINE, CAPLUS, BIOSIS, EMBASE, WPIDS

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,597,719 A (FREED et al) 28 January 1997, abstract.	1-2

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

\* Special categories of cited documents:

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*B\* earlier document published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

\*A\* document member of the same patent family

Date of the actual completion of the international search

16 NOVEMBER 1999

Date of mailing of the international search report

22 DEC 1999

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
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Authorized officer

EVERETT WHITE

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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/15062

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-2

Remark on Protest

☐  
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING**

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1, drawn to a method of identifying a target protein and a modifier.

Group II, claim(s) 2 and 3, drawn to a pharmaceutical composition and a method of treating an individual suffering from an inflammatory condition.

Group III, claim(s) 2 and 4, drawn to a pharmaceutical composition and a method of treating an individual suffering from an undesirable immune response or immunological condition.

Group IV, claims 2 and 5, drawn to a pharmaceutical composition and a method of treating an individual suffering from a bacterial infection.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for more than one species to be searched, the appropriate additional search fees must be paid. The species are as follows:

(a) Formula I; (b) Formula II; (c) Formula III; (d) Formula IV; (e) Formula V; (f) Formula VI; (g) Formula VII; (h) Formula VIII; (i) Formula IX; (j) Formula X; (k) Formula XI; (l) Formula XII; (m) Formula XIII; (n) Formula XIV; (o) Formula XV; (p) Formula XVI; (q) Formula XVII; (r) Formula XVIII; and (s) Formula XIX.

The inventions listed as Groups I and II do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The compounds used in the method of identifying a compound that modulates intermolecular interaction between a target protein and a modifier as disclosed in Group I are not limited to the compounds used for the method of treating an individual suffering from an inflammatory condition of Group II.

The inventions listed as Groups I and III do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The compounds used in the method of identifying a compound that modulates intermolecular interaction between a target protein and a modifier as disclosed in Group I are not limited to the compounds used for the method of treating an individual suffering from an undesirable immune response or immunological condition of Group III.

The inventions listed as Groups I and III do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The compounds used in the method of identifying a compound that modulates intermolecular interaction between a target protein and a modifier as disclosed in Group I are not limited to the compounds used for the method of treating an individual suffering from a bacterial infection of Group IV.

The inventions listed as Groups II and III do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The compounds used in the method of treating an individual suffering from an inflammatory condition as disclosed in Group II are not limited to the compounds used for the method of treating an individual suffering from an undesirable immune response or immunological condition of Group III.

The inventions listed as Groups II and IV do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The compounds used in the method of treating an individual suffering from an inflammatory condition as disclosed in Group II are not limited to the compounds used for the method of treating an individual suffering from a bacterial infection of Group IV.

The inventions listed as Groups III and IV do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The compounds used in the method of treating an individual suffering from an undesirable immune response or immunological condition as disclosed in Group III are not limited to the compounds used for the method of treating an individual suffering from a bacterial infection of Group IV.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/15062

The species listed above do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Each of the species sets forth a structure which is clearly different from the other species. A reference containing one of the recited species in the instant application cannot be used to reject a claim containing a different species of the instant application.